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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/430,412	10/29/1999	PAUL ALBERT	2268UO-1	7273

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SHERIDAN ROSS PC
1560 BROADWAY
SUITE 1200
DENVER, CO 80202

EXAMINER	
HAYES, ROBERT CLINTON	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 04/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/430,412	ALBERT ET AL.	
	Examiner	Art Unit	
	Robert C. Hayes, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *5-8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-8* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 October 1999* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/10/00*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I (claims 1-4) in Paper No. 9/11/03 is acknowledged. The traversal is on the ground(s) that "the method claims of Group III relate to the use of the DNA of Group I", and "[t]herefore, the subject matter of Groups I and III is so small that a thorough search of the subject matter of Group I will be sufficient to examine the claims of Group III". This is not found persuasive because the method of Group III is distinct from the DNA product of Group I, because test samples from patients with depression or other mental illnesses, labeling protocols, PCR and DNA sequencing procedures for detecting/ determining DNA sequences, as well as primers and a spectrum of mutated DNAs (i.e., different DNA molecules) are all required in the method of Group III, but are not required for the product of Group I, which alternatively is directed toward a specific mutated DNA product with reduced repressor function. Moreover, as previously made of record in Paper No: 10, different uses can exist for the polynucleotides of Group I, such as gene therapy, which is not required in the method of Group III; thereby, being distinct for the reasons made of record. A serious burden further exists because the different goals and method steps required for the claims of Group III are not required for examination of the products of Group I, and for the reasons made of record in Paper No: 10. Thus, the requirement is still deemed proper and is therefore made FINAL.

Claims 5-8 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9/11/03.

This application contains claims 5-8 drawn to an invention nonelected with traverse in Paper No. 9/11/03. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Drawings

2. New corrected drawings are required in this application for the reasons indicated on PTO form 948. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Claim Rejections - 35 U.S.C. § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-4 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. For example, the current recitation of "a DNA sequence..." encompasses all naturally occurring polynucleotides comprising the 5-HTIA receptor gene; thereby, not involving the hand of man to isolate or purify the polynucleotide. It is suggested that amending claim 1 to "an isolated DNA molecule [sequence]..." should obviate this

rejection; along with deletion of the recitations of "sequence" in claims 2-4 to reflect more conventional claim language.

Claim Rejections - 35 U.S.C. § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

No written description is provided in the instant specification as to what structurally constitutes nucleotide sequences *comprising* unknown and undescribed promoter sequences, 5'- or 3'-flanking or enhancer or silencer regions, or any other undescribed genomic DNA sequences that "contain [undescribed] mutation[s] in the repressor region of the 5-HT1A receptor *gene*", in that no sequences for these different molecules are described; nor can they be reasonably visualized by one skilled in the art, especially when the ends of a 5-HT1A "gene" are unknown, and not described. Second, the genus of such mutated DNA promoter sequences, as currently claimed, encompass generic 5'-, 3'-flanking, enhancer, silencer, and additional promoter sequences from different species, which alternatively would be expected by the skilled artisan to have widely divergent functional properties. In contrast, the instant specification solely describes the *human* 5-HT1A promoter of *SEQ ID NO: 1* with a single specific substitution, in

which no other promoter sequences, nor functional mutations therein, are described. In other words, one skilled in the art can not reasonably visualize or predict what critical nucleotide residues would structurally characterize the genus of polynucleotides that constitute a mutated 5-HT1A receptor gene; thereby, not reasonably meeting the written description requirements under 35 U.S.C. 112, first paragraph. See MPEP 2163.

It is suggested that amending the claims to "an isolated DNA molecule consisting of SEQ ID NO: 1 and a G-C substitution mutation at position 2422 of SEQ ID NO:1, wherein said mutation in the repressor region of this 5-HT1A receptor DNA results in a reduction in the repressor function leading to enhanced 5-HT1A receptor expression" should obviate this rejection, and be allowable.

5. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific isolated DNA molecule consisting of SEQ ID NO: 1 with specific and defined mutations, does not reasonably provide enablement for any nucleic acid sequence that comprises structurally uncharacterized 5-HT1A receptor promoter sequences, nor for any biological functional equivalent molecules with no specific recited structural characteristics. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The name "a mutation in the repressor region of the 5-HT1A receptor gene", or the recitations of "single or multiple base pair change, an inversion, a deletion and an insertion", or open-ended definitions that encompass any biologically functional equivalent of a 5-HT1A

receptor gene sets forth no structural characteristics and little functional characterization. In contrast, the specification fails to teach which particular nucleotide residues are critical for any 5-HT1A receptor gene promoter's function in any cell, nor how to distinguish such from any different DNA sequence that possesses none of the desired functions of the instant invention. The specification solely discloses the human 5-HT1A receptor gene promoter of SEQ ID NO: 1. The specification fails to disclose any other 5-HT1A receptor gene promoter DNA molecule, except for one with a G-C substitution, nor discloses what structurally constitutes any different nucleotide sequence, as encompassed by the current claims. Moreover, any random "mutation" to the disclosed human promoter sequence of SEQ ID NO 1 would reasonably be expected by the skilled artisan to either eliminate expression of the species/cell-specific expression of the 5-HT1A receptor protein, or alter its expression pattern such that one could not distinguish the resultant expression pattern from any other protein. For example, LeClerc et al. teach random mutations to promoter sequences normally result in either an altered or inactive promoter sequence. Thus, the lack of guidance within the specification as to what critical nucleotides are involved in appropriate 5-HT1A receptor gene promoter function would prevent one skilled in the art at the time of filing Applicants' invention to reasonably determine what "single or multiple base pair change, an inversion, a deletion and an insertion" would constitute a functional invention, or even what specific nucleotides structurally constitute a functional human 5-HT1A receptor gene since none are recited, without requiring undue experimentation to discover how to make and use Applicants' invention.

6. Claims 2-4 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite and/or incomplete for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Because no reference sequence (i.e., SEQ ID NO: 1) is recited in the claims, it is unclear what the recited position numbers for mutated residues exactly mean, because for example, any addition or deletion to SEQ ID NO: 1 (for which the claims are not limited towards) changes the position number of the nucleotide residues to be changed, and because any different 5-HT1A sequence (especially as it relates to open claim language), would reasonably have different numbers of nucleotide residues; thereby, making these current claims indefinite.

Claim Rejections - 35 U.S.C. § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Parks et al (IDS Ref #AF; 1996).

Parks et al. teach isolation of the human and murine 5-HT1A receptor gene promoters, which contain "multiple base pair changes/deletions", etc. in the putative region of "about -3438 to about -393 from the ATG codon of the 5-HT1A receptor gene", for example, when compared to SEQ ID NO: 1 (pg. 4420; Fig. 1; as it relates to claims 1-3); thereby, inherently resulting in a

reduction in the repressor function leading to enhanced 5-HT1A receptor expression; absent evidence to the contrary. In that the murine 5-HT1A DNA sequence contains a G-C substitution at position -1017 (i.e., residue # 242 of SEQ ID NO: 1) along with "multiple base pair changes/deletions", etc. when compared to SEQ ID NO: 1, the limitations of claim 4 are met.

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (571) 272-0885. The examiner can normally be reached on Monday through Thursday, and alternate Fridays, from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (571) 272-0887. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
April 14, 2004